

**REMARKS**

Claims 1, 3-6, 16 and 17 are all the claims pending in the application.

The claims have been amended to delete various members of Markush groups and to replace the term “derivative” with “compound.” No new matter is added.

The title has been amended as suggested by the Examiner.

**II. Detailed Action**

**A. Claim Objections**

1. Claim 1 is objected to because the fourth line from the last line in claim 1 recites, “r is 1 or 2).” The Examiner states that “2)” should be replaced with “2.”

This objection is traversed, respectfully. The close parentheses “)” after the “2” is needed to complete the open parentheses “(“ in line 4 of claim 1.

2. Claim 17 is objected to because, according to the Examiner, claim 17 is a substantial duplicate of claims 1-8 and 16, the only difference being a statement of intended use, which is not given material weight.

This objection is overcome by amending claim 17 to delete the use and to recite a composition.

3. The Examiner further states that claims 1-18 were amended in the Preliminary Amendment filed July 5, 2006, but the claims submitted on July 19, 2007 do not indicate the proper status identifiers based on the Preliminary Amendment.

Applicants believe that there is some mistake on the part of the Patent Office. Applicants’ records do not show that a paper was filed on July 19, 2007. On the other hand, the transaction history in PAIR for the present application indicates that a Request for Foreign

Priority was made on July 19, 2007 and this is believed to have come from the Patent Office.

Clarification is requested if this objection is maintained.

4. Finally, the Examiner states that claims 9-15, 16 (in part) and 18, are drawn to an invention non-elected with traverse in the Response filed July 7, 2008 and a complete reply to the Final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

In response, all non-elected claims and subject matter have been canceled.

**B. Claim Rejections - 35 U.S.C. § 112**

1. Claims 1-8 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

**(a) “Derivative”**

The Examiner states that the word “derivative” is vague.

This aspect of the rejection has been overcome by replacing the word “derivative” with “compound.”

**(b) “An antagonist for CRF receptors”**

The Examiner states that in claim 17, the preamble is drawn to a compound but the claim language embraces compositions, i.e. “active ingredient.” The Examiner states that if Applicants intend a composition, then an excipient, carrier and/or diluent should be added to the claim and if Applicants intend a compound, claim 17 does not further limit claims 1-16 as presently written.

Claim 17 has been amended to recite a composition.

2. Claims 1-8, 16 and 17 are rejected under 35 U.S.C. §112, first paragraph, as being non-enabled for isomers, hydrates and prodrugs.

The amendments to the claims overcome this rejection by deleting the recitation of isomers, hydrates and prodrugs

**C. Claim Rejections - 35 USC § 103**

Claims 1-8 and 17 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nakazato et al. (US 6,852,732 B2).

According to the Examiner, the instant invention claims compounds of formula (I), wherein Ar = 2,4-dichlorophenyl; Y= nitrogen; n= 0; m=0; X= hydroxyl, cyano, CO<sub>2</sub>R<sup>8</sup> or CONR<sup>9</sup>R<sup>10</sup>; R<sup>6</sup>= methyl; R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>7</sup>, R<sup>4</sup> and R<sup>5</sup> = hydrogen; and the nitrogen ring is a 6-membered unsaturated nitrogen ring, piperidine, and simple compositions thereof.

The Examiner relies on the disclosure of Nakazato et al. as teaching compounds of formula (I), wherein Ar= 2,4,6-trimethylphenyl; Y= nitrogen; n= 0; m=0; X= 2-ethyl; R<sup>6</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup>= methyl; R<sup>7</sup>, R<sup>4</sup> and R<sup>5</sup> = hydrogen; and the nitrogen ring is a 6-membered nitrogen ring, piperidyl-3-ene, and simple compositions thereof. See columns 47-48, compounds 11-01-11-03 and column 66, claim 3.

According to the Examiner, the difference between the compounds of the reference and the compounds of the instant Application is the piperidine ring is unsaturated whereas the corresponding piperidine ring is saturated in the present compounds. The Examiner further states that the reference teaches that the nitrogen ring can be saturated or unsaturated, see column 2, subformula (III), and therefore the unsaturated and saturated ring systems are alternatively

useable. Thus, the Examiner concludes that the present claims are rendered obvious by Nakazato et al.

For the following reasons the rejection is traversed and/or overcome, respectfully.

The Examiner's description of the invention is incorrect in that the nitrogen ring according to the invention is saturated.

The Examiner's assessment of the cited reference is also incorrect. Ar and X according to Nakazato et al. are not 2,4,6-trimethylphenyl and 2-ethyl, respectively.

More specifically, in the instant invention, the cyclic amino group is a saturated piperidine ring.

In contrast, Nakazato et al. teaches that in sub-formula (III) at column 2 the nitrogen ring can be saturated or unsaturated; however, the compounds referred by the Examiner contain an unsaturated piperidine ring. Further, Nakazato et al. teaches in column 2 that the substituent should be different depending on the nature of the 6-membered nitrogen ring (whether it is unsaturated (formula (II)) or saturated (formula (III))).

Specifically, according to the teachings of Nakazato et al., when the 6-membered nitrogen ring is saturated as indicated by formula (III), the substituent should be;



This substituent is structurally entirely different from that defined in the instant claims.

In view of the fact that Nakazato et al. discloses structurally distinct substituents for each of formula (II) and formula (III), one of ordinary skill in the art would not have been motivated

to interchange the substituents with a reasonable expectation of obtaining compounds having the intended activity.

Moreover, in the phrase bridging columns 64-65, Nakazato et al. reports the test results of evaluating the affinity of the compounds to the CRF receptor. As seen in the list of effective compounds, none of the compounds in Table 11 exhibits an  $IC_{50}$  value of 500 nM or less.

Furthermore by the amendments made to the present claims, the substituents  $-CO_2R^8$  and  $-CONR^9R^{10}$  have been deleted from the definition of X so that the instantly claimed compounds are those having X = cyano or hydroxyl.

In conclusion, it is submitted that, based on the disclosure of compounds 11-01 to 11-03 disclosed in Nakazato et al. containing a tetrahydropyridine (= 6-membered unsaturated nitrogen ring) substituted with  $-CONH_2$ , one of ordinary skill in the art would not have been motivated:

- (1) to change the tetrahydropyridine ring to a 6-membered saturated nitrogen ring,  
and
- (2) to change the substituent  $-CONH_2$  to  $-(CR^1R^2)_m(CHR^3)_nX$ , wherein X is cyano or hydroxyl",

with a reasonable expectation of obtaining compounds showing a desirable CRF receptor antagonist activity.

Accordingly, the Examiner is requested, respectfully, to reconsider and remove the rejection.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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**23373**

CUSTOMER NUMBER

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